



SEQUENCE LISTING

<110> Saksena, Anil K

Girijavaliabhan, Viyyor M

Lovey, Raymond G

Jao, Edwin

Bennett, Frank

McCormick, Jinping L

Pike, Russell E

Bogen, Stephane L

Liu, Yi-Tsung

Arasappan, Ashok

Pinto, Patrick A

Njoroge, F George

Ganguly, Ashit

<120> NOVEL PEPTIDES AS NS3-SERINE PROTEASE INHIBITORS OF HEPATITIS C VIRUS

<130> IN01157K-US

<140> 09/909,062

<141> 2001-07-19

<150> 60/220,109

<151> 2000-07-21

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<170> PatentIn version 3.1

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<223> acetyl-Glu(OtBu)

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<223> Glu(OtBu)

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Xaa Xaa Val Val Pro Xaa Gly
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<211> 7

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<223> Glu(OtBu)

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<223> norvaline-(CHOH)

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<223> Gly-allylamide

<400> 52

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1 5

<210> 53

<211> 7

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<222> (6)..(6)

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<223> Gly-allylamide

<400> 53

Xaa Xaa Val Val Pro Xaa Xaa
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<211> 7

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<222> (6) .. (6)

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<220>

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<223> Gly-allylamide

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Xaa Glu Val Val Pro Xaa Xaa
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<211> 7

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<223> Gly-allylAm

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<223> Gly-2PhEtAm

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<210> 57

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<223> Gly-PropAm

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Glu Glu Val Val Pro Xaa Xaa
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<210> 58

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<210> 59

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<223> Gly-iPrAm

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Glu Glu Val Val Pro Xaa Xaa
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<210> 60

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<223> Gly (OAllyl)

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Glu Glu Val Val Pro Xaa Xaa
1 5

<210> 61

<211> 7

<212> PRT

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<223> synthetic peptide

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<222> (7)..(7)

<223> Gly-(OAllyl)

<400> 61

Xaa Xaa Val Val Pro Xaa Xaa
1 5

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<222> (7)..(7)

<223> Gly-(OAllyl)

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Xaa Xaa Val Val Pro Xaa Xaa
1 5

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<212> PRT

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<222> (7) .. (7)

<223> Gly-(OAllyl)

<400> 63

Glu Glu Val Val Pro Xaa Xaa
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<210> 64

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<222> (6) .. (6)

<223> norvaline-C(=O)

<220>

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<210> 65

<211> 7

<212> PRT

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Glu Glu Val Val Pro Xaa Xaa
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<210> 66

<211> 7

<212> PRT

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<223> Gly-(OAllyl)

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Glu Glu Val Val Pro Xaa Xaa
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<210> 67

<211> 7

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<222> (6) .. (6)

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<222> (7) .. (7)

<223> Gly-(OAllyl)

<400> 67

Glu Glu Val Val Pro Xaa Xaa
1 5

<210> 68

<211> 7

<212> PRT

<213> Artificial Sequence

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<223> Gly-(Propynyl)-C(=O)

<220>

<221> MISC_FEATURE

<222> (7)..(7)

<223> Gly-(Oallyl)

<400> 68

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<210> 69

<211> 7

<212> PRT

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<223> Gly-OEt

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<210> 70

<211> 7

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<223> Gly-(Oallyl)

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<222> (6) .. (6)

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<221> MISC_FEATURE

<222> (7) .. (7)

<223> Gly-(OAllyl)

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<210> 72

<211> 7

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<220>

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<223> Gly-(OtBu)

<400> 72

Glu Glu Val Val Pro Xaa Xaa
1 5

<210> 73

<211> 7

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<223> synthetic peptide

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<223> ACETYLATION

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<222> (6) .. (6)

<223> Gly(Allyl) -C(=O)

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<223> Gly- (OEt)

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1 5

<210> 74

<211> 7

<212> PRT

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<223> synthetic peptide

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<223> ACETYLATION

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<222> (6) .. (6)

<223> Cys(Me) -C(=O)

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<221> MISC_FEATURE

<222> (7) .. (7)

<223> Gly-OMe

<400> 74

Glu Glu Val Val Pro Xaa Xaa
1 5

<210> 75

<211> 7

<212> PRT

<213> Artificial Sequence

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<223> synthetic peptide

<220>

<221> MOD_RES

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<223> ACETYLTATION

<220>

<221> MISC_FEATURE

<222> (5) .. (5)

<223> Gly (N-Bu(4NH₂, 4-CO₂H))

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<221> MISC_FEATURE

<222> (6) .. (6)

<223> norvaline-C(=O)

<400> 75

Glu Glu Val Val Xaa Xaa Gly
1 5

<210> 76

<211> 7

<212> PRT

<213> Artificial Sequence

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<223> ACETYLTATION

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<222> (5)..(5)

<223> Gly (N-Bu(4NH₂, 4-COOH))

<220>

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<222> (6)..(6)

<223> norvaline-C(=O)

<400> 76

Glu Glu Val Val Xaa Xaa Gly
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<210> 77

<211> 7

<212> PRT

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<223> synthetic peptide

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<223> ACETYLATION

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<222> (5)..(5)

<223> Gly(N-Bu(4NH₂, 4-COOH))

<220>

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<223> norvaline-C(=O)

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Glu Glu Val Val Xaa Xaa Gly
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<210> 78

<211> 7

<212> PRT

<213> Artificial Sequence

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<223> ACETYLTATION

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<222> (5)..(5)

<223> Gly(N-Et(CO₂H))

<220>

<221> MISC_FEATURE

<222> (6)..(6)

<223> norvaline-C(=O)

<400> 78

Glu Glu Val Val Xaa Xaa Gly
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<210> 79

<211> 7

<212> PRT

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<223> synthetic peptide

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<223> ACETYLATION

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<222> (5)..(5)

<223> Gly(N-EtPh(3,4 diOMe))

<220>

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<222> (6)..(6)

<223> norvaline-C(=O)

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<210> 80

<211> 7

<212> PRT

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<221> MOD_RES

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<223> ACETYLATION

<220>

<221> MISC_FEATURE

<222> (5) .. (5)

<223> Gly(N-Pe(5-NH2,5-CO2H))

<220>

<221> MISC_FEATURE

<222> (6) .. (6)

<223> norvaline-C(=O)

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<210> 81

<211> 7

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<223> ACETYLATION

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<222> (5) .. (5)

<223> Gly(N-Et(NHBz))

<220>

<221> MISC_FEATURE

<222> (6) .. (6)

<223> norvaline-C(=O)

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Glu Glu Val Val Xaa Xaa Gly
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<210> 82

<211> 4

<212> PRT

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<223> Fmoc-Val

<220>

<221> MISC_FEATURE

<222> (2)..(2)

<223> Gly(N-Et (NH-Boc))

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<222> (3)..(3)

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<222> (4)..(4)

<223> Gly-PAM resin

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Xaa Xaa Xaa Xaa
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<210> 83

<211> 4

<212> PRT

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<220>

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<222> (2) .. (2)

<223> Gly(N-Et(NHBz))

<220>

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<222> (3) .. (3)

<223> norvaline-(dspc)

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<222> (4) .. (4)

<223> Gly-PAM resin

<400> 83

Xaa Xaa Xaa Xaa

1

<210> 84

<211> 7

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<222> (5)..(5)

<223> Gly(N-Et(NHBz))

<220>

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Glu Glu Val Val Xaa Xaa Gly
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<210> 85

<211> ?

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<220>

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<222> (5) .. (5)

<223> Gly(N-Et(NHBzl(3-OPh)))

<220>

<221> MISC_FEATURE

<222> (6) .. (6)

<223> norvaline-(C=O)

<400> 85

Glu Glu Val Val Xaa Xaa Gly
1 5

<210> 86

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<223> ACETYLATION

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<222> (5) .. (5)

<223> Gly(N-Prop(NHBz))

<220>

<221> MISC_FEATURE

<222> (6) .. (6)

<223> norvaline- (C=O)

<400> 86

Glu Glu Val Val Xaa Xaa Gly
1 5

<210> 87

<211> 6

<212> PRT

<213> Artificial Sequence

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<223> synthetic peptide

<220>

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<223> AMIDATION

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<221> MISC_FEATURE

<222> (6) .. (6)

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<400> 87

Glu Glu Val Val Pro Xaa
1 5

<210> 88

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

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<220>

<221> MISC_FEATURE

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<223> Glu(OtBu)

<220>

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<222> (6) .. (6)

<223> norvaline-(CHOH)-CONH2

<400> 88

Xaa Xaa Val Val Pro Xaa
1 5

<210> 89

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic peptide

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<223> acetyl-Glu(OtBu)

<220>

<221> MISC_FEATURE

<222> (2)..(2)

<223> Glu(OtBu)

<220>

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<222> (6)..(6)

<223> norvaline-(C=O)-CONH2

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Xaa Xaa Val Val Pro Xaa
1 5

<210> 90

<211> 6

<212> PRT

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<220>

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<222> (6) .. (6)

<223> norvaline--(C=O)--CONH2

<400> 90

Glu Glu Val Val Pro Xaa
1 5

<210> 91

<211> 6

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<223> ACETYLATION

<220>

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<222> (6) .. (6)

<223> norvaline- (C=O) -Am

<400> 91

Glu Glu Val Val Pro Xaa
1 5

<210> 92

<211> 7

<212> PRT

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<223> ACETYLATION

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<222> (5) .. (5)

<223> Pro(4t-MeNHBzl(3-OPh))

<220>

<221> MISC_FEATURE

<222> (6) .. (6)

<223> norvaline- (C=O)

<400> 92

Glu Glu Val Val Xaa Xaa Gly
1 5

<210> 93

<211> 7

<212> PRT

<213> Artificial Sequence

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<223> synthetic peptide

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<221> MISC_FEATURE

<222> (2) .. (2)

<223> Glu(OtBu)

<220>

<221> MISC_FEATURE

<222> (5) .. (5)

<223> Pro(4t-MeNHfmoc)

<220>

<221> MISC_FEATURE

<222> (6) .. (6)

<223> norvaline-(dpSC)

<220>

<221> MISC_FEATURE

<222> (7) .. (7)

<223> Gly-PAM resin

<400> 93

Xaa Xaa Val Val Xaa Xaa Xaa
1 5

<210> 94

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic peptide

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<223> acetyl-Glu(OtBu)

<220>

<221> MISC_FEATURE

<222> (2) .. (2)

<223> Glu(OtBu)

<220>

<221> MISC_FEATURE

<222> (5) .. (5)

<223> Pro(4t-MeNH2)

<220>

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<223> norvaline-(dspc)

<220>

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<222> (7) .. (7)

<223> Gly-PAM resin

<400> 94

Xaa Xaa Val Val Xaa Xaa
1 5

<210> 95

<211> 7

<212> PRT

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<223> Glu(OtBu)

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<222> (5) .. (5)

<223> Pro(4t-MeNHBzl(3-OPh))

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<222> (7) .. (7)

<223> Gly-PAM resin

<400> 95

Xaa Xaa Val Val Xaa Xaa Xaa
1 5

<210> 96

<211> 7

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<223> synthetic peptide

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<223> ACETYLATION

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<222> (5)..(5)

<223> Pro(4t-MeNHBzl(3-OPh))

<220>

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<222> (6)..(6)

<223> norvaline-(C=O)

<400> 96

Glu Glu Val Val Xaa Xaa Gly
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<210> 97

<211> 7

<212> PRT

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<220>

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<223> ACETYLATION

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<222> (5) .. (5)

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<220>

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<222> (6) .. (6)

<223> norvaline- (C=O)

<400> 97

Glu Glu Val Val Xaa Xaa Gly
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<210> 98

<211> 7

<212> PRT

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<222> (5) .. (5)

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<220>

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<222> (6) .. (6)

<223> norvaline-(C=O)

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Glu Glu Val Val Xaa Xaa Gly
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<210> 99

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<222> (5)..(5)

<223> Pro(4t-MeNH-Fmoc)

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<222> (6)..(6)

<223> norvaline-(C=O)

<400> 99

Glu Glu Val Val Xaa Xaa Gly
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<210> 100

<211> 7

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<223> Pro(4t-MeNHSO₂Ph)

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<223> norvaline- (C=O)

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Glu Glu Val Val Xaa Xaa Gly
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<210> 101

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<223> Pro(4t-MeUreaPh)

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Glu Glu Val Val Xaa Xaa Gly
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<222> (5) .. (5)

<223> Pro(4t-NH-Fmoc)

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<223> norvaline- (C=O)

<400> 102

Glu Glu Val Val Xaa Xaa Gly
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<210> 103

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<222> (5)..(5)

<223> Pro(4t-NHBZ1)

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<222> (6)..(6)

<223> norvaline-(C=O)

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Glu Glu Val Val Xaa Xaa Gly
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<210> 104

<211> 4

<212> PRT

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<220>

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<223> Fmoc-Val

<220>

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<222> (2) .. (2)

<223> Pro(4t-NHBzl)

<220>

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<222> (3) .. (3)

<223> norvaline-(dpSC)

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<222> (4) .. (4)

<223> Gly-PAM resin

<400> 104

Xaa Xaa Xaa Xaa

1

<210> 105

<211> 5

<212> PRT

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<220>

<223> synthetic peptide

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<223> Fmoc-Val

<220>

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<222> (3) .. (3)

<223> Pro(4t-NHBzl)

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<222> (4) .. (4)

<223> norvaline-(dpse)

<220>

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<222> (5) .. (5)

<223> Gly-PAM resin

<400> 105

Xaa Val Xaa Xaa Xaa
1 5

<210> 106

<211> 6

<212> PRT

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<220>

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<220>

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<222> (1)..(1)

<223> Fmoc-Glu(OtBu)

<220>

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<222> (4)..(4)

<223> Pro(4t-NHBzl)

<220>

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<223> norvaline-(dpSC)

<220>

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<222> (6) .. (6)

<223> Gly-PAM resin

<400> 106

Xaa Val Val Xaa Xaa Xaa
1 5

<210> 107

<211> 7

<212> PRT

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<222> (2) .. (2)

<223> Glu(OtBu)

<220>

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<222> (5) .. (5)

<223> Pro(4t-NHBzl)

<220>

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<222> (6) .. (6)

<223> norvaline- (dpSC)

<220>

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<222> (7) .. (7)

<223> Gly-PAM resin

<400> 107

Xaa Xaa Val Val Xaa Xaa Xaa
1 5

<210> 108

<211> 7

<212> PRT

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<222> (5) .. (5)

<223> Pro(4t-NHBzl)

<220>

<221> MISC_FEATURE

<222> (6)..(6)

<223> norvaline-(C=O)

<400> 108

Glu Glu Val Val Xaa Xaa Gly
1 5

<210> 109

<211> 7

<212> PRT

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<223> ACETYLATION

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<222> (5)..(5)

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<220>

<221> MISC_FEATURE

<222> (6) .. (6)

<223> norvaline- (C=O)

<400> 109

Glu Glu Val Val Xaa Xaa Gly
1 5

<210> 110

<211> 7

<212> PRT

<213> Artificial Sequence

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<223> ACETYLATION

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<222> (5) .. (5)

<223> Pro(4t-NHBzl(4-OPh))

<220>

<221> MISC_FEATURE

<222> (6) .. (6)

<223> norvaline- (C=O)

<400> 110

Glu Glu Val Val Xaa Xaa Gly
1 5

<210> 111

<211> 7

<212> PRT

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<223> ACETYLTATION

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<222> (5) .. (5)

<223> Pro(4t-NHBzl(3-OPh))

<220>

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<222> (6) .. (6)

<223> norvaline- (C=O)

<400> 111

Glu Glu Val Val Xaa Xaa Gly
1 5

<210> 112

<211> 7

<212> PRT

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<223> ACETYLATION

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<222> (5)..(5)

<223> Pro(4t-NHBzl(3,4-OMe))

<220>

<221> MISC_FEATURE

<222> (6)..(6)

<223> norvaline-(C=O)

<400> 112

Glu Glu Val Val Xaa Xaa Gly
1 5

<210> 113

<211> 7

<212> PRT

<213> Artificial Sequence

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<222> (1) .. (1)

<223> ACETYLATION

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<222> (5) .. (5)

<223> Pro(4t-NHBzl(4F))

<220>

<221> MISC_FEATURE

<222> (6) .. (6)

<223> norvaline- (C=O)

<400> 113

Glu Glu Val Val Xaa Xaa Gly
1 5

<210> 114

<211> 7

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<223> Pro(4t-NHiBoc)

<220>

<221> MISC_FEATURE

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<223> norvaline.. (C=O)

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<210> 115

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<223> ACETYLATION

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<222> (5) .. (5)

<223> Pro(4t-NHSO2Ph)

<220>

<221> MISC_FEATURE

<222> (6) .. (6)

<223> norvaline- (C=O)

<400> 115

Glu Glu Val Val Xaa Xaa Gly
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<210> 116

<211> 7

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<222> (5) .. (5)

<223> Pro(4t-NHSO2Ph(4-OMe))

<220>

<221> MISC_FEATURE

<222> (6) .. (6)

<223> norvaline- (C=O)

<400> 116

Glu Glu Val Val Xaa Xaa Gly
1 5

<210> 117

<211> 7

<212> PRT

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<221> MISC_FEATURE

<222> (5) .. (5)

<223> Pro(4t-UreaPh)

<220>

<221> MISC_FEATURE

<222> (6) .. (6)

<223> norvaline- (C=O)

<400> 117

Glu Glu Val Val Xaa Xaa Gly
1 5

<210> 118

<211> 7

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<223> ACETYLTATION

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<222> (5) .. (5)

<223> Pro(4t-UreaPh(4-OMe))

<220>

<221> MISC_FEATURE

<222> (6) .. (6)

<223> norvaline- (C=O)

<400> 118

Glu Glu Val Val Xaa Xaa Gly
1 5

<210> 119

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

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<223> ACETYLTATION

<220>

<221> MISC_FEATURE

<222> (6)..(6)

<223> norvaline- (C=O)

<400> 119

Glu Glu Val Val Pro Xaa
1 5

<210> 120

<211> 6

<212> PRT

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<222> (1) .. (1)

<223> acetyl-Glu(OtBu)

<220>

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<222> (2) .. (2)

<223> Glu(OtBu)

<220>

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<222> (6) .. (6)

<223> norvaline-(CHOH)-OEt

<400> 120

Xaa Xaa Val Val Pro Xaa
1 5

<210> 121

<211> 6

<212> PRT

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<223> acetyl-Glu(OtBu)

<220>

<221> MISC_FEATURE

<222> (2) .. (2)

<223> Glu(OtBu)

<220>

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<222> (6) .. (6)

<223> norvaline-(CHOH)-carboxylic acid

<400> 121

Xaa Xaa Val Val Pro Xaa
1 5

<210> 122

<211> 6

<212> PRT

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<223> ACETYLATION

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<222> (6)..(6)

<223> norvaline-(CHOH)-carboxylic acid

<400> 122

Glu Glu Val Val Pro Xaa
1 5

<210> 123

<211> 6

<212> PRT

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<222> (6)..(6)

<223> norvaline-(C=O)-carboxylic acid

<400> 123

Glu Glu Val Val Pro Xaa
1 5

<210> 124

<211> 6

<212> PRT

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<223> ACETYLATION

<220>

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<222> (6)..(6)

<223> norvaline-(C=O)-OH

<400> 124

Glu Glu Val Val Pro Xaa
1 5

<210> 125

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> NS5A-NS5B junction sequence

<220>

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<222> (7) .. (7)

<223> alanine or proline

<220>

<221> MISC_FEATURE

<222> (8) .. (8)

<223> norvaline

<400> 125

Asp Thr Glu Asp Val Val Xaa Xaa
1 5

<210> 126

<211> 5

<212> PRT

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<220>

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<222> (2) .. (2)

<223> D-Gla

<220>

<221> MISC_FEATURE

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<223> I- (Cha)

<400> 126

Asp Xaa Leu Xaa Cys
1 5

<210> 127

<211> 8

<212> PRT

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<220>

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<220>

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<222> (1) .. (1)

<223> ACETYLATION

<220>

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<222> (8)..(8)

<223> norvaline

<400> 127

Asp Thr Glu Asp Val Val Ala Xaa
1 5

<210> 128

<211> 8

<212> PRT

<213> Artificial Sequence

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<220>

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<222> (1)..(1)

<223> ACETYLATION

<220>

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<222> (8)..(8)

<223> norvaline

<400> 128

Asp Thr Glu Asp Val Val Pro Xaa
1 5

<210> 129

<211> 6

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<223> ACETYLATION

<220>

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<222> (6)..(6)

<223> norvaline- (C=O)-iPrAm

<400> 129

Glu Glu Val Val Pro Xaa
1 5

<210> 130

<211> 7

<212> PRT

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<220>

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<222> (7) .. (7)

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<222> (6) .. (6)

<223> norvaline- (C=O)

<400> 130

Glu Glu Val Val Pro Xaa Gly
1 5

<210> 131

<211> 7

<212> PRT

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<220>

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<222> (1) .. (1)

<223> ACETYLATION

<220>

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<223> Gly(Ph)

<220>

<221> MISC_FEATURE

<222> (6) .. (6)

<223> norvaline-(C=O)

<400> 131

Glu Glu Val Xaa Pro Xaa Gly
1 5

<210> 132

<211> 7

<212> PRT

<213> Artificial Sequence

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<223> ACETYLTATION

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<222> (5) .. (5)

<223> Pro(4t-O-2AcOH)

<220>

<221> MISC_FEATURE

<222> (6) .. (6)

<223> norvaline- (C=O)

<400> 132

Glu Glu Val Val Xaa Xaa Gly
1 5

<210> 133

<211> 7

<212> PRT

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<222> (5) .. (5)

<223> thio-Pro

<220>

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<222> (6) .. (6)

<223> norvaline- (C=O)

<400> 133

Glu Glu Val Val Xaa Xaa Gly
1 5

<210> 134

<211> 7

<212> PRT

<213> Artificial Sequence

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<222> (5)..(5)

<223> Pro-(4t-NH2)

<220>

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<223> norvaline-(C=O)

<400> 134

Glu Glu Val Val Xaa Xaa Gly
1 5

<210> 135

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic peptide

<220>

<221> MOD_RES

<222> (1) .. (1)

<223> ACETYLATION

<220>

<221> MISC_FEATURE

<222> (3) .. (3)

<223> Ala(1-Np)

<220>

<221> MISC_FEATURE

<222> (6) .. (6)

<223> norvaline- (C=O)

<400> 135

Glu Glu Xaa Val Pro Xaa Gly
1 5

<210> 136

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic peptide

<220>

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<221> MISC_FEATURE

<222> (3)..(3)

<223> Ala(2-Np)

<220>

<221> MISC_FEATURE

<222> (6)..(6)

<223> norvaline-(C=O)

<400> 136

Glu Glu Xaa Val Pro Xaa Gly
1 5

<210> 137

<211> 7

<212> PRT

<213> Artificial Sequence

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<223> synthetic peptide

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<222> (1) .. (1)

<223> ACETYLATION

<220>

<221> MISC_FEATURE

<222> (3) .. (3)

<223> Phe(alpha-Me)

<220>

<221> MISC_FEATURE

<222> (6) .. (6)

<223> norvaline- (C=O)

<400> 137

Glu Glu Xaa Val Pro Xaa Gly
1 5

<210> 138

<211> 7

<212> PRT

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<223> synthetic peptide

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<222> (1) .. (1)

<223> ACETYLATION

<220>

<221> MISC_FEATURE

<222> (6) .. (6)

<223> norvaline- (C=O)

<400> 138

Glu Glu Val Leu Pro Xaa Gly
1 5

<210> 139

<211> 7

<212> PRT

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<223> synthetic peptide

<220>

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<222> (1) .. (1)

<223> ACETYLATION

<220>

<221> MISC_FEATURE

<222> (4) .. (4)

<223> Gly(t-Bu)

<220>

<221> MISC_FEATURE

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<400> 139

Glu Glu Val Xaa Pro Xaa Gly
1 5

<210> 140

<211> 7

<212> PRT

<213> Artificial Sequence

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<222> (6)..(6)

<223> norvaline-(C=O)

<400> 140

Glu Glu Val Ser Pro Xaa Gly
1 5

<210> 141
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<223> ACETYLATION

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<400> 141
Glu Glu Val Thr Pro Xaa Gly
1 5

<210> 142
<211> 7
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<223> norleucine

<220>

<221> MISC_FEATURE

<222> (6)..(6)

<223> norvaline- (C=O)

<400> 142

Glu Glu Val Xaa Pro Xaa Gly
1 5

<210> 143

<211> 7

<212> PRT

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<220>

<223> synthetic peptide

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